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Revisiting the "forever chemicals", PFOA and PFOS exposure in drinking water

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Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS), known as the most detected per- and polyfluoroalkyl substances (PFAS) in various environmental compartments, have been associated with plastic pollution and endocrine dysfunction. Over the past 180 years (1839–2019), numerous emerging contaminants have been identified, with PFOA and PFOS receiving considerable attention based on scientific evidence and publications. Between 2018 and 2019, PFOA and PFOS experienced a relatively high increase rate of 18.8% and 13.6%, respectively. While developed countries have made progress in establishing stringent guidelines, developing and underdeveloped countries often lack regulations and mechanisms to address emerging PFAS. Furthermore, advancements in PFAS removal technologies are needed to improve their efficacy and feasibility. The establishment of regulatory compliances, along with exposure assessment and risk characterization, is essential for providing precautionary advice on water source protection, water supply security, health risks, treatment efficiency, and contamination forecasting. However, a more comprehensive approach and database for evaluating exposure and risks are still imperative to effectively combat PFAS contamination in drinking water. Therefore, this review aims to enhance environmental monitoring and management practices in response to the global crisis of PFAS contamination. The analysis of Needs, Approaches, Benefits, and Challenges (NABC) is grounded in the current trends of PFAS in the environment and human exposure through drinking water.

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INTRODUCTION

Per- and polyfluoroalkyl substances (PFAS) are a class of highly fluorinated chemicals that have been widely synthesized and utilized since the 1940s in various industrial practices and consumer products, acting as surfactants, flame retardants, additives, lubricants, and pesticides; generated as by-products, residues, and intermediates in various processes[1–3]. Due to their multiple carbon–fluorine (C–F) bonds, PFAS exhibit enhanced chemical and thermal stability, rendering them persistent and resistant to degradation[4]. They are also hydrophobic and lipophobic, capable of bioaccumulation and sorption, and can be transported through various modes of action in the environment, thereby posing toxicity to organisms[5]. The environmental fate of PFAS is influenced by their structural properties, including functional groups, carbon chain length, hydrophobicity, and lipophobicity[5,6]. With over 4000 compounds belonging to this class and being utilized in various industries and products as polymers and additives, PFAS, commonly referred to as "forever chemicals", are suspected environmental contaminants and endocrine disruptors, although only a small number is currently monitored and regulated[7,8].

In the early 1960s, the revelation of human exposure to environmental contaminants stemming from PFAS manufacturing and application marked the emergence of a global contamination crisis[9]. PFAS are extensively utilized for their "non-stick" properties and their ability to reduce surface tension, rendering them valuable in repelling water and oil, preventing stains, and modifying surface chemistry[8]. Due to their widespread use as key components in aqueous film-forming foams (AFFF), PFAS contamination sites continue to be discovered worldwide, particularly in the vicinity of airports and military bases where AFFF is frequently used for firefighting and training activities[3,8]. PFAS exhibits a wide range of toxic effects, including developmental toxicity, genotoxicity, carcinogenicity, hepatotoxicity, reproductive toxicity, immunotoxicity, cytotoxicity, neurotoxicity, and hormonal toxicity[10]. Primarily, they have been associated with elevated risks of cancer, immune responses, metabolic syndromes, developmental issues, and reproductive effects[8]. These adverse effects stem from their ability to disrupt the endocrine system through interactions with nuclear receptors, classifying PFAS as potential endocrine disruptors[10,11].

Perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS) are two of the most used PFAS compounds in various applications. Although they have been phased out globally, they persist in the environment and are listed under the Stockholm Convention on Persistent Organic Chemicals[12]. The continuous concern regarding PFOA and PFOS has prompted research on their replacement, such as perfluorohexanoic acid (PFHxA), perfluorohexane sulfonic acid (PFHxS), hexafluoropropylene oxide dimer acid (HFPO-DA or GenX), and 6:2 chlorinated polyfluoroalkyl ether sulfonic acid (6:2 Cl-PFAES or commercially known as F-53B), which have garnered great interest[13–16]. Moreover, the International Agency for Research on Cancer (IARC) has classified PFOA as "possibly carcinogenic to humans"[17]. Epidemiological studies have reported a strong association between both PFOA and PFOS and testicular and kidney cancer; however, conclusive results require long-term follow-up studies with large cohorts that have significant exposure contrasts[18]. Additionally, it is important to consider that different isomers of each PFAS may exhibit variations in toxicity[19]. Risk estimation based solely on traditional endpoints such as growth, reproduction, and mortality may not adequately capture PFAS toxicity. Advanced molecular biological

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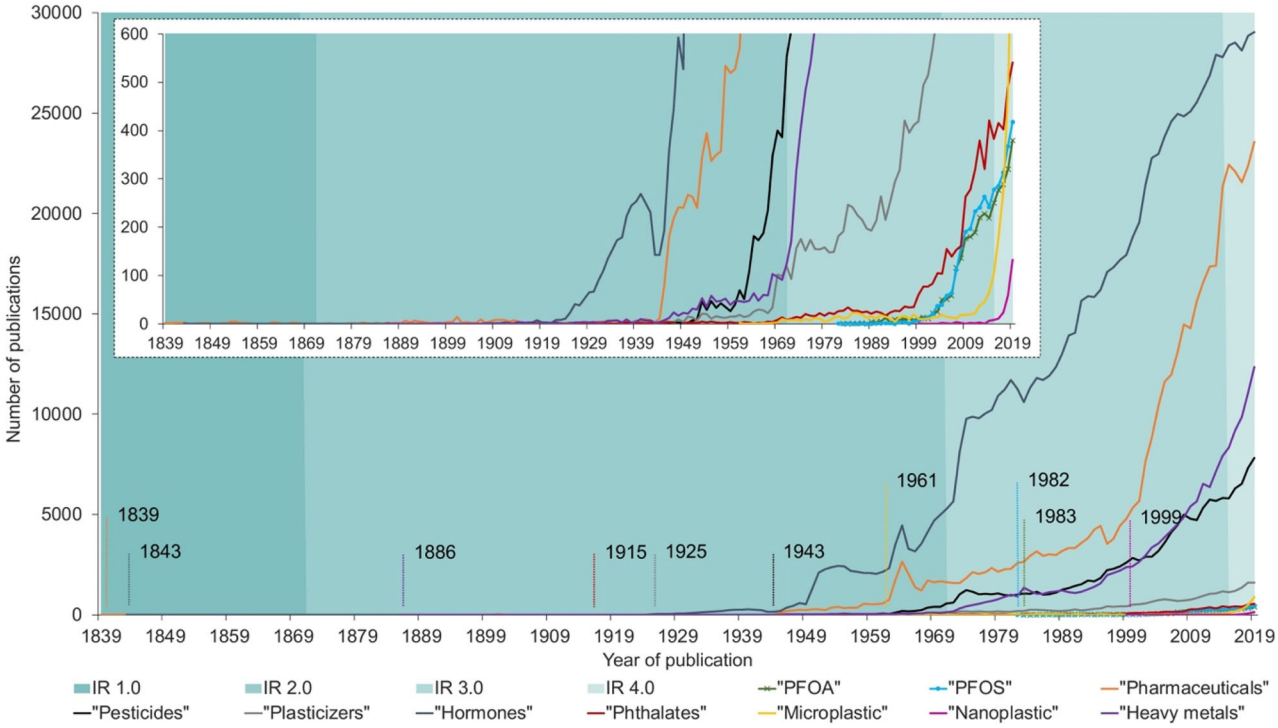


Fig. 1 Research interests in emerging contaminants with potential endocrine dysfunction effects over the years in relation to the industrial revolution. Between the years 1839 and 2019, PFOA and PFOS have emerged as the most concerning chemical contaminants, as evidenced by the scientific attention and research devoted to them. Data are based on the Scopus search system.

approaches that utilize more sensitive endpoints to generate sublethal information, enabling a more effective assessment of the environmental impact of PFAS[20].

The discharge of environmental contaminants into surface water, release into the air, and leaching into soil and groundwater has become a predominant concern due to industrialization[11]. The widespread use of PFAS has contributed to the contamination of drinking water[1,21,22]. Analysis of data on PFAS levels in community tap water in Massachusetts reveals a trend of increasing contamination, with total fluorinated compounds exhibiting a 5- to 320-fold rise over 25 years, and up to 94% of these compounds remaining unquantified (unknown PFAS)[23]. The primary source of human exposure, residential drinking water (mean concentration of 3.55 µg/L), was initially identified with the detection of PFOA in human blood (mean concentration of 423 µg/L) among the non-occupational exposed United States population between 2002 and 2005[24]. In a study by Hu et al.[23], tap water was found to contribute to 2.2–34% of plasma concentrations for the five tested PFAS compounds in female participants (aged between 43 and 69) of the Nurses' Health Study. The emergence of contaminants over a span of 180 years (1839 to 2019) started with pharmaceuticals (Fig. 1). Scientific attention focused on PFOA and PFOS, as evidenced by research findings and publications, indicating their significance among the investigated chemical contaminants in relation to the industrial revolution. Between the years 2018 and 2019, PFOA and PFOS exhibited a relatively high increase rate of 18.8% and 13.6%, respectively, while other contaminants such as pharmaceuticals (5.4%), plasticizers (6.8%), pesticides (−0.5%), hormones (0.7%), phthalates (10.0%), and heavy metals (11.7%) experienced different rates, and despite the significant research interest in physical contaminants (microplastic: 81.1%; nanoplastic: 123.7%), based on analysis conducted using the Scopus database (Fig. 1).

PFAS are intricately connected to the global issue of plastic pollution, as they co-occur with microplastics and other additives and polymers[25]. In some cases, polymeric PFAS can exist as microplastics, resulting from the breakdown of fluoropolymers, for instance, polyvinyl fluoride (PVF) and polytetrafluorethylene (PTFE)[26]. Additionally, PFAS are commonly employed as coatings on synthetic textiles and plastic components, which can degrade into fiber- or particle-based macro-, meso-, or microplastics during production, application, and disposal processes. Furthermore, non-PFAS microplastics, such as polyvinyl chloride (PVC), can connect with PFAS during manufacturing. PFAS can be released from side-chain fluorinated polymer groups present in various plastics, paper, and textile products[27]. Schellenberger et al.[28] reported the release of side-chain fluorinated polymer-containing microplastic fibers from functional textiles during washing, whereby fluorinated side chains were then cleaved from the polymer and transformed into short-chain PFAS. The interaction between PFAS and microplastics is predominantly driven by hydrophobic interaction, influenced by the characteristics of PFAS (e.g., hydrophobicity and ionic properties), physicochemical and polymeric properties of microplastics, and environmental factors (pH, salinity, temperature, dissolved organics, etc.)[25,29]. Under specific conditions, desorption of PFAS from microplastics can occur. This phenomenon highlights the role of microplastic as transport vectors for these chemical contaminants in the environment and their potential impact on human exposure.

Over the past few decades, research attention has been directed towards understanding the implications of PFOA and PFOS, particularly in the context of drinking water quality (Fig. 2a). Analysis using the Scopus search system indicates that concerns regarding drinking water quality originated as early as 1851 with the publication of the first article addressing lead poisoning. Since then, the scope of research has expanded to include other contaminants, including metals, minerals/nutrients, microorganisms, and disinfectants/disinfection by-products. Although investigations into PFOA and PFOS began in the 1980s, their presence in drinking water was not widely recognized until the 2000s. The issue has gardened attention, particularly in the United States, which was the initial hotspot with continuous contamination and

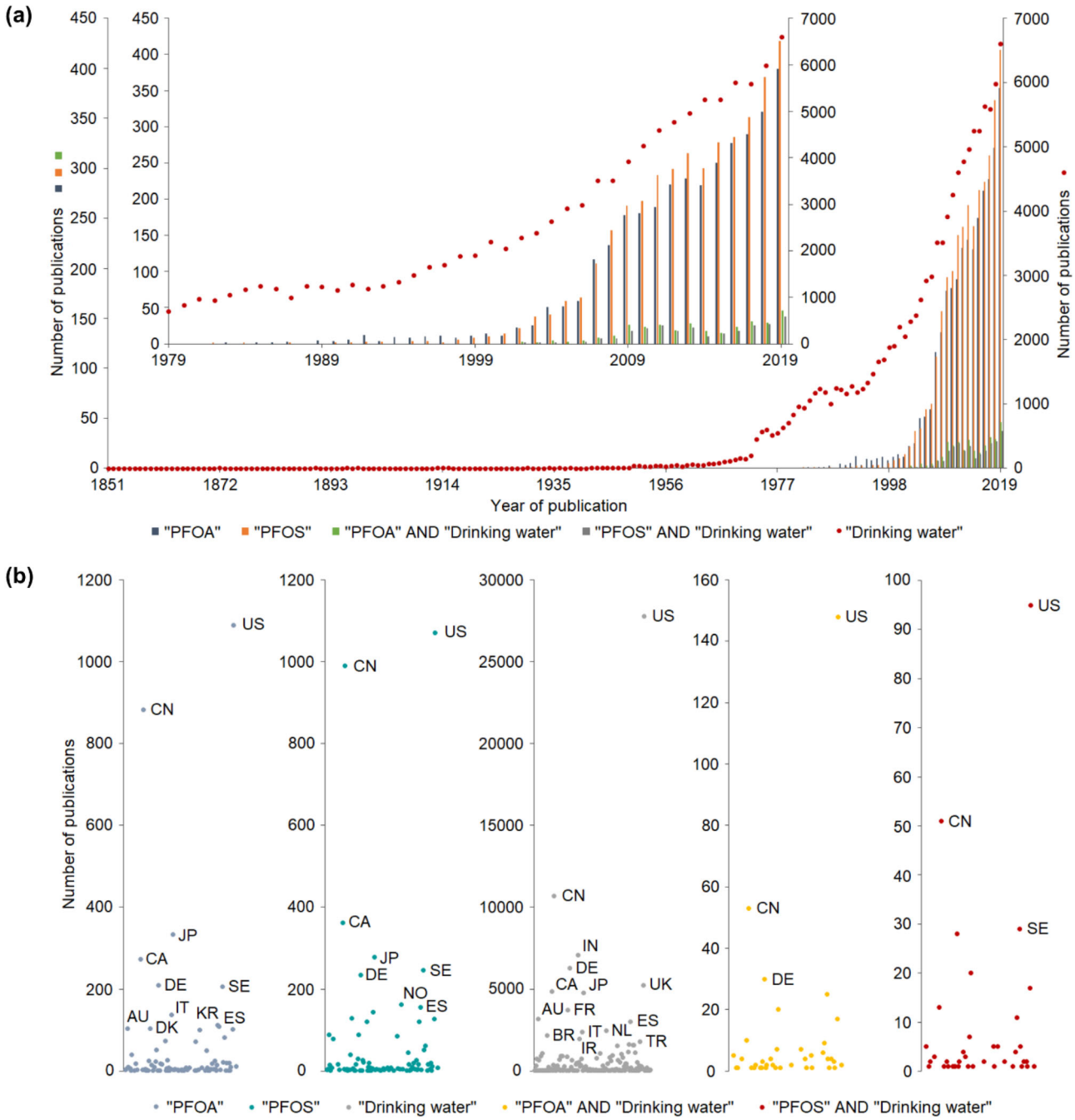


Fig. 2 Trend of research interest in PFOA and PFOS related to drinking water issues. a Annual number of publications; the increasing interest is driven by the potential human exposure and associated health outcomes, primarily attributed to regular water consumption as the key source of exposure. **b** Geographical distribution of publications; countries labeled as such make significant contributions to the top 10% of publications, reflecting their past and ongoing contamination levels. Data are based on the Scopus search system.

detection in both human and animal organisms[8,9,21,30]. Furthermore, the United States remains at the forefront of research endeavors investigating PFAS contamination in drinking water (Fig. 2b). It is crucial not to overlook the fact that this issue is of global significance, with varying levels of contamination in drinking water supplies (both tap and bottled water) across continents, regardless of the countries' development status. In terms of exposure effects, ingestion of PFAS through drinking water has been found to result in higher levels of exposure compared to other prevalent routes (e.g., diet and consumer products)[31]. Even at low levels of contamination, PFAS concentrations in drinking water have been shown to lead to a substantial increase in PFAS levels in blood serum, exceeding 100 times on average.

Thus, the objective of this review is to provide a comprehensive overview of the pathways through which PFAS are released into the environment and subsequently expose humans to their potential health effects. This review also aims to elucidate the contamination of global drinking water sources (including surface water and groundwater) and drinking water supplies (both tap water and bottled water), as well as the efficiency of treatment methods and the existing regulations concerning PFAS in drinking water. By doing so, this review intends to enhance our understanding of the quality issues associated with drinking water,

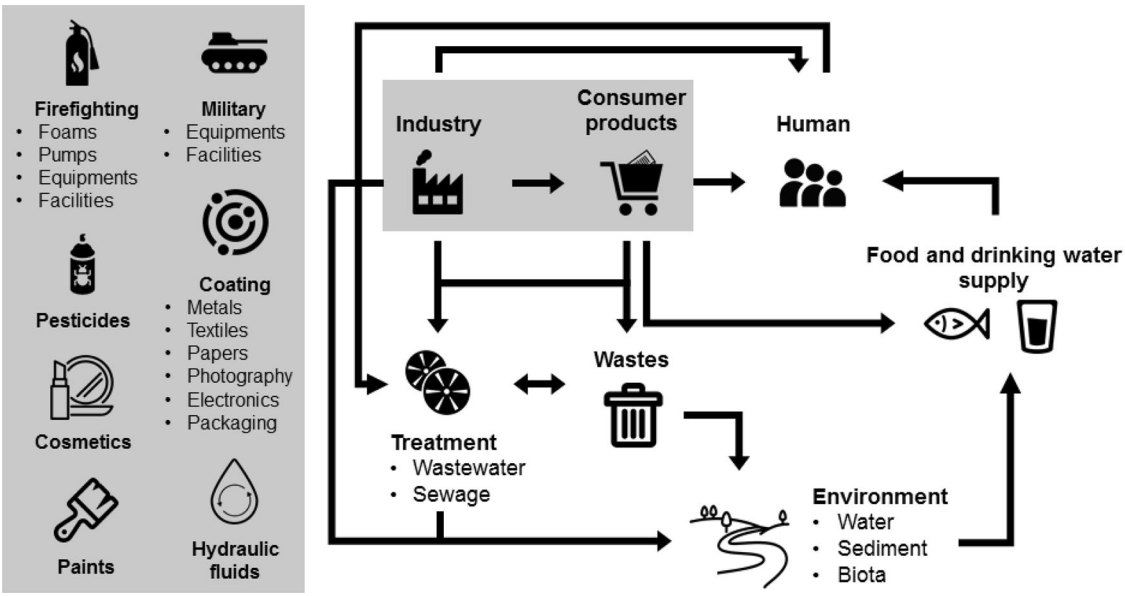


Fig. 3 Release and exposure pathways of PFAS in the environment and humans. The widespread utilization of PFAS has resulted in their pervasive occurrence in the environment, with contamination levels and distribution influenced by both anthropogenic and natural stressors. The presence of PFAS in the ecosystem signifies their entry into diverse terrestrial and aquatic food chains and webs, ultimately reaching humans as the final consumers.

particularly in relation to the hazards posed by PFAS, with a specific focus on PFOA and PFOS, and their implications for human health through daily water consumption. It is anticipated that this article will serve as a valuable resource for addressing and monitoring the ongoing global drinking water crisis.

RELEASE ESTIMATION, EXPOSURE PATHWAYS, AND HEALTH EFFECTS

Since the 2000s, growing concerns regarding the environmental pollution and health implications associated with legacy PFAS, particularly PFOA and PFOS, have prompted efforts to regulate their manufacturing practices and establish monitoring guidelines. Notably, the major producer of PFAS, 3 M Company, voluntarily discontinued the production of PFOA and PFOS in the early 2000s[32,33]. Similarly, DuPont ceased the production and use of PFOA in 2013 as part of its agreement with the United States Environmental Protection Agency (US EPA), and other companies worldwide are gradually phasing out production as well[33]. More recently, 3M company announced its intention to completely halt all PFAS manufacturing by the end of 2025[34]. However, despite the gradual phase-out of long-chain PFAS by major manufacturers and the presence of regulations in the United States, Japan, and Western Europe, new manufacturers, primarily located in continental Asia, have begun producing long-chain PFAS and their precursors[32,35]. Concurrently, the US EPA, manufacturers, and various organizations have intensified their monitoring and testing efforts for PFAS in the environment and in human populations. Nonetheless, PFAS still persists in various environmental compartments, including air, wastewater, sewage, surface water, groundwater, sediments, plants, and biota[8]. The release and persistence of PFAS in the environment occur during production and manufacturing processes (e.g., chemical, electronic, photographic, military, aviation, agricultural, packaging, and textile industries), product usage (e.g., consumer goods, firefighting events, and training activities), disposal (e.g., landfill), and chemical or product discharge[1,21,22,36]. It is worth noting that although PFAS are not manufactured in Ghana, surface water in the country have been found to be contaminated, in which the contamination is attributed to the importation and local use of various PFAS-containing products, such as furniture, cooking utensils, clothing, plastics, food packaging, medical equipment, motor oil additives, firefighting foams, and paints[37]. Furthermore, improper disposal of waste materials from these products has led to the contamination of open drainages and water bodies. Figure 3 illustrates the release and exposure pathways of PFAS to humans.

Occupational exposure to PFAS is typically higher compared to general exposure[38,39]. Among the various PFAS, perfluoroalkyl acids exhibit relatively low volatility (PFOA: 3.16×10^{-1}; PFOS: 2.00×10^{-3} mm Hg at 25 °C), but ionic PFAS in the air has a high likelihood of adsorbing onto particulate matter, followed by atmospheric transportation and deposition, with seasonal variation playing a role[40]. Inhalation of indoor dust, total suspended particles, and consumption of drinking water are the main routes of exposure to PFAS among occupational workers[39,41]. PFAS are present in both gaseous (PFOA: 1.25–64.28 pg/m^3; PFOS: ≤ 14.71 pg/m^3) and particulate (PFOA: 2.76–205.54 pg/m^3; PFOS: 0.52–8.21 pg/m^3) phases, and the partitioning between the gaseous and particulate phases is influenced by meteorological conditions, such as air temperature and pressure, in China[42]. Consequently, humans can be exposed to PFOA and PFOS at levels 1.94–60.2 and 0.30–4.22 pg/kg/day, respectively, through inhalation. However, PFAS exposure is not limited to occupational settings but also occurs in the general population. Contaminated drinking water and food supply are potential sources of oral and dermal exposure to PFAS, with inhalation exposure occurring to a lesser extent. In Hong Kong, airborne particles sampled in kindergartens showed a maximum concentration of PFOA at 1896 pg/m^3 (mean concentration = 358 pg/m^3), resulting in a maximum estimated daily intake of 711 pg/kg/day (mean = 134 pg/kg/day) through inhalation among the children aged 4–6 years[43]. Dermal exposure is another route of exposure to PFAS through consumer products, which can occur in offices, households, and transportation settings, particularly in populations with diverse product use patterns[44–47]. Notably, Post et al.[31] emphasized that drinking water is a predominant source of contamination in the general population, surpassing other sources such as food and consumer products.

PFAS concentrations in worldwide sewage treatment plants have been found to range up to 465.4, 5663.3 ng/L, and 7304.9 ng/g dry weight in influent, effluent, and sludge, respectively, indicating the inefficiency of secondary biological treatment with a negative removal rate[48]. The spatial variation of PFAS emissions through wastewater discharges within the Danube River catchment is influenced not only by treatment type and coverage but also by population size, with higher emissions of PFOA and PFOS estimated in densely populated urban areas[49]. Additionally, the problem is exacerbated by inadequate wastewater treatment, as PFAS are released into water bodies during the discharge of domestic and industrial effluents and can further spread through runoff and leaching at waste disposal sites and landfills due to their limited removal in wastewater and sewage treatment processes (Fig. 3). These compounds, particularly the long-chain PFAS, exhibit high persistence, sorption, and stability in the environment, leading to biotransformation, bioaccumulation, and biomagnification effects within the ecosystem[5]. Although short-chain PFAS are generally more water-soluble than long-chain PFAS, they can still adsorb to soil and sediment particles and be transported through air or water, showing resistance to biological and chemical degradation[5,50].

The practice of irrigation, whether with reclaimed or contaminated non-reclaimed water, as well as the application of fertilizers such as biosolids, can contribute to additional pathways of PFAS contamination in soil, leading to the uptake of PFAS by plants, including crops, and organisms like earthworms, with varying uptake and translocation rate in different plant species[51–55]. Notably, PFOA and PFOS are end products of PFAS transformation, typically originating from precursors of PFOA and PFOS and other perfluoroalkyl acids, and these compounds are released into the environment during biodegradation and biotransformation processes within soil–organism, soil–plant, and soil–organism–plant systems[54,55]. PFAS can enter various terrestrial and aquatic food chains, ultimately reaching humans as the final consumers. When organisms ingest microplastics, PFAS are released and retained in their tissues and cells, contributing to the accumulation within the food chain[56,57]. PFAS exposure persists and accumulates in the environment and food chains, typically detected at levels ranging from pg/g to ng/g, while direct exposure through product usage can gradually decrease through changes in chemical production[8]. Domingo and Nadal[58] highlighted that dietary intake is the primary route of human exposure to PFAS, particularly among the general population, with detections of PFAS in the food supply, both raw and processed, across various regions including Asia, North America, European countries, as well as Brazil, Saudi Arabia, Spain, and Serbia.

Furthermore, migration from packaging materials serves as an alternate source of PFAS in food and beverages, resulting in direct human exposure[47]. PFAS have been frequently detected in food-contact materials such as boxes, bags, wrappers, cups, and tablewares across multiple countries[59–63]. Efforts aligned with Sustainable Development Goal 12, which aims to ensure sustainable consumption and production patterns, have focused on adopting and implementing green concepts to reduce costs (economic, environmental, and social), enhance economic competitiveness, promote sustainable management of resources, energy, chemicals, and wastes, and minimize waste generation. However, eco-friendly and recycled materials, including plant fiber-based paper tableware like sugarcane and reed pulp fiber, available in markets such as Columbus, Ohio, United States, and China, have been found to contain emerging contaminants, including PFAS[63]. Notably, PFOA was the most frequently detected PFAS (90%), with concentrations ranging up to 103 ng/g. Additionally, Ernstoff et al.[64] highlighted the potential trade-offs between chemical exposure and other environmental impacts and emphasized the need to incorporate chemical toxicity into the life cycle impact assessment of food packaging. The United States Food and Drug Administration (US FDA) is actively expanding its understanding of the occurrence and exposure of PFAS in the food supply and regulates PFAS as direct and indirect food additives under the Code of Federal Regulations and the Food Contact Notification list, addressing their addition or migration into food along the production chain. Prominent restaurant chains such as Restaurant Brands International and McDonald's have made commitments to eliminate the use of PFAS-containing packaging[65,66]. The United States, such as Maine and Washington, have banned the use of all PFAS in food contact materials, and Denmark has prohibited the use of PFAS in paper and paperboard food packaging[67]. Government policymakers have taken action to ban PFAS in various products, including food packaging, firefighting foam, carpets, and rugs.

Moreover, human exposure to PFAS through regular water consumption is primarily influenced by drinking water contamination[39]. The contamination in drinking water is closely associated with both point and non-point sources of environmental water contamination[21,36]. For instance, the Daegu Basin and Ansan/Shiheung Basin in Korea, which are dominated by textile and metal industries, respectively, have shown relatively high levels of PFOA and PFOS (730 and 550 ng/L, respectively) in surface water, associated with a strong connection between the contamination of local PFAS emission sources and tap water contamination in this area[68]. China, being a country with substantial PFOA and PFOS industries, is estimated to release 40 t/yr of PFOA and 70 t/yr of PFOS into the environment, with 87% and 86%, respectively originating from industrial emissions (the remainder from domestic emissions)[69]. Approximately 77.5% of PFOA and 90% of PFOS emissions (31 and 63 t/yr, respectively) are released into surface water, which is the common raw water source for treatment before consumption (the remainder is released into the soil). The varying physicochemical properties of PFAS isomers have implications not only on their isomeric distribution in raw water sources and toxicokinetics but also on the efficiency of treatment processes[70]. Qu et al.[71] demonstrated negative removal rates of PFOA and PFOS in a conventional drinking water treatment plant, ranging from −10% to −2% and −14% to 8.2%, respectively. Similar patterns have been observed for other emerging organic contaminants, such as pharmaceuticals and drugs, phthalates, plasticizers, pesticides, and hormones, in the global drinking water supply system[11]. Due to the unique characteristics of PFOA and PFOS, including functional groups, carbon chain length, hydrophobicity, isomeric structure, and precursor transformation, most conventional and advanced treatment technologies have been found to be ineffective in substantially removing them. The causes underlying this ineffectiveness are explored in detail in Section 3, highlighting the need for the development of diverse removal protocols.

Recently, there has been growing concern regarding the dynamics, loadings, and partitioning of emerging contaminants in the drinking water supply system, particularly when their occurrence and distribution vary in different housing types such as high-rise and landed houses[72]. Figure 4 demonstrates the levels of PFOA and PFOS in global drinking water sources and supplies, revealing comparably high contamination levels in the United States and Sweden across the continents (Fig. 4). The maximum concentration of PFOA was observed in both drinking water sources (11,000 ng/L) and supplies (4300 ng/L) in the United States, while the highest level of PFOS was detected in Swedish drinking water sources (2280 ng/L) and supplies (8000 ng/L)[73–75]. These countries, renowned for their extensive PFAS manufacturing and consumption activities, have become major contamination hotspots[8,9,21,30,76]. Additionally, they are among the top countries actively involved in monitoring and managing PFOA and/or PFOS (Fig. 2b). Although PFAS production has been phased out in primary manufacturing countries, there has been a substantial increase in production in developing nations[32,35]. In Ghana, tap

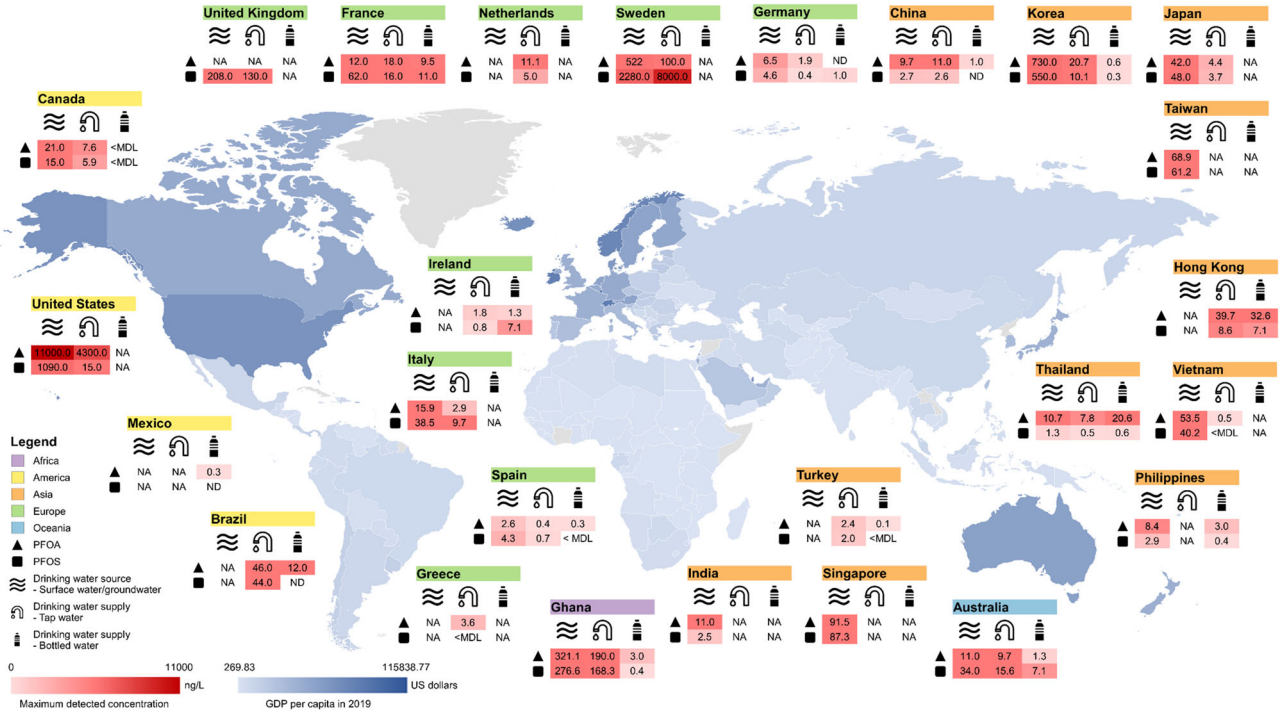


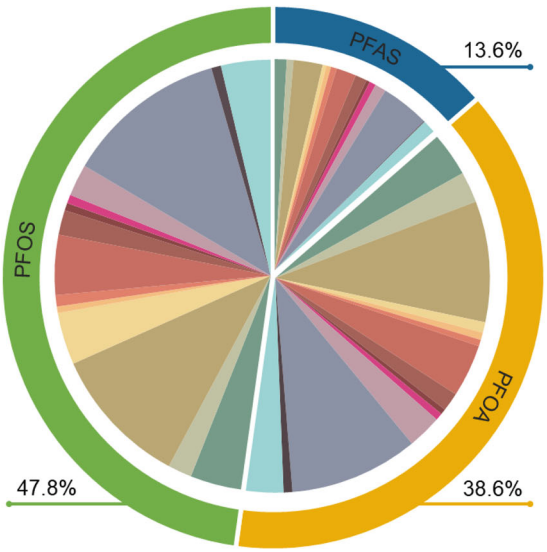
Fig. 4 GDP and the maximum detected levels of PFOA and PFOS in global drinking water sources and supplies. The global issue is predominantly attributed to ongoing pollution from various sources, and incomplete removal methods, all compounded by inadequate monitoring and management practices, with potential impacts influenced by GDP. Data are based on[37,43,68,71,73–75,77–80,135,154–171]. Base map courtesy of mapchart.net (http://www.mapchart.net).

water sourced from River Pra and River Kakum, which have been dammed for drinking water treatment and supplied to adjacent communities under Integrated Water Resources Management by the Water Resources Commission, exhibits relatively high concentrations of PFOA (190 ng/L) and PFOS (168.3 ng/L)[37]. In Brazil, PFAS exposure through drinking water has been reported based on the detection of PFAS in tap water (PFOA: 46 ng/L; PFOS: 44 ng/L) and bottled water (PFOA: 12 ng/L) (Fig. 4). A study by Schwanz et al.[77] found variations in PFAS levels among bottled water samples from different markets (Brazil, France, and Spain), with PFOS only detected in samples from France (1.6–11 ng/L), and significantly higher mean total PFAS concentrations in Brazilian tap water (55 ng/L; $p < 0.05$). Korean tap water samples exhibited the highest mean concentration of PFOA (12.87 ng/L, with a maximum concentration of 20.7 ng/L) among all PFAS, which was nearly 80 times higher than the mean concentration of PFOA (0.16 ng/L, with a maximum concentration of 0.6 ng/L) detected in the bottled water samples, indicating possible PFAS contamination in the drinking water source, particularly surface water[78]. Similarly, PFOA was found at much higher concentrations compared to other PFAS in the Hong Kong water supply (tap water: 39.7 ng/L; bottled water: 32.6 ng/L), followed by PFOS (tap water: 8.6 ng/L; bottled water: 7.1 ng/L)[43]. Interestingly, bottled water in Thailand contained higher levels of PFAS (especially PFOA and PFOS) compared to tap water[79,80]. This disparity in contaminant levels implies that bottled materials may have an impact on the quality of water[77].

The contamination issues are a result of inadequate monitoring and management of emerging contaminants in the environmental system, which is characterized by ongoing scientific efforts, relatively low public awareness, continuous source pollution, incomplete removal, and unregulated distribution[81]. Additionally, factors such as population size, treatment efficiency, and gross domestic product (GDP) can influence the receiving and discharge of PFAS in both domestic and industrial wastewater treatment plants[49,82]. The significant and modest positive correlation observed between PFAS levels in tap water and GDP ($r = 0.457$; $p < 0.01$) can be attributed to the local economic development level, particularly economic wealth and purchasing power[83]. Consequently, the emission and contamination of PFAS are potentially influenced by GDP, which is inextricably linked to the consumption, production, use, and disposal of PFAS-containing products. While striving to achieve the United Nations Sustainable Development Goals, finding a balance among the goals is crucial in efforts to decouple environmental degradation from economic growth and protect public health. This issue is further highlighted by the limited knowledge of PFAS occurrence in many countries across worldwide, as depicted in Fig. 4, suggesting that the associated risks may have been underestimated.

PFAS exhibit remarkable bioaccumulation in the human body (cells, blood, and breast milk), with the accumulation levels being influenced by different types of PFAS, types of human tissues, life stages, and genders[8,30,74,76,84–86]. Notably, the lung demonstrated higher levels of PFAS accumulation compared to the liver, brain, kidney, and bone tissues, while PFOS was found to be more prevalent in the liver and PFOA was predominantly detected in bone[86]. Moreover, the central nervous system exhibited lower PFAS detection compared to other tissues[84]. Interestingly, a study highlighted a significantly higher accumulation of PFOA in placentas carrying male fetuses compared to those carrying female fetuses based on the placenta-to-serum ratio (5.6% higher). Furthermore, maternal serum exhibited higher PFAS loading, followed by cord serum and breast milk, with PFOA and PFOS being the predominant PFAS in all matrices[87].

In general, PFOA tends to have a shorter elimination time compared to PFOS[8,74]. There have been increasing temporal trends in most PFAS concentrations in adult blood serum from the 1970s to the 2000s, followed by a decreasing trend from the 2000s to the 2010s, whereby these differences in bioaccumulation can be attributed to changes in age demographics and manufacturing



Number of publications

	PFAS	PFOA	PFOS
Body weight	44	159	184
Cancer	25	112	86
Cell	107	438	506
Heart	14	38	188
Bone	17	27	23
Nervous	22	23	41
Endocrine	73	191	216
Immune	43	67	89
Respiratory	13	20	27
Skin	24	26	31
Kidney	41	123	115
Metabolism	179	467	581
Genotoxicity	3	32	35
Reproductive	48	135	178

Fig. 5 Publications on the health outcomes associated with PFOA and PFOS. Metabolic disruption was the most extensively investigated health outcome compared to other effects, followed by cell toxicity and endocrine dysfunction. Additionally, studies focused more on exposure to PFOS rather than PFOA. Data are based on the Scopus search system.

processes[30,74,88–91]. Additionally, there is a sex difference, with PFOS being excreted more rapidly in females compared to males, although the difference in PFOA elimination is marginal[74]. Factors such as menstruation and pregnancy (including lactation, cord-blood and placental transfer, and breastfeeding) are associated with lower serum PFAS levels in adult females (particularly those of childbearing age) compared to males[89,92]. Furthermore, maternal serum concentrations of PFAS are influenced by factors such as maternal age, education, breastfeeding duration, and pre-pregnancy body mass index[89]. Similar temporal concentration trends of PFAS have also been observed in human breast milk[76].

Simultaneously, the excretion routes for mothers serve as the exposure routes for fetuses, infants, and children to PFAS. PFAS accumulate in the placenta throughout gestation and are transferred to fetal organs, with PFAS loading increasing with fetal age[84]. Furthermore, exposure to PFOA and PFOS through breast milk has been found to be higher than prenatal exposure *in utero*[87]. In contrast to the decreasing temporal trends observed in adulthood, there is an increase in serum PFAS levels at the beginning of infancy or childhood due to the high dependence on breastmilk as the primary source of exposure, which is influenced by the duration of breastfeeding[93–95]. Various health organizations, such as the World Health Organization, American Academy of Pediatrics, and Academy of Breastfeeding Medicine, recommend exclusive breastfeeding from birth to 6 months of age, followed by continued breastfeeding up to 2 years of age or longer with complementary food based on mutual desire between the mother and infant. Maternal exposure can even result in higher PFAS levels in nursing infants compared to their mothers[95–97]. This trend is followed by a decrease after breastfeeding cessation, resulting in reduced exposure from the primary source and lower exposure from other sources. Nevertheless, PFAS body burdens in children remain unchanged or increase with age, indicating the parallel influence of temporal changes and growth dilution on children's exposure[93].

The effects of PFAS in humans are highly associated with prenatal exposure and encompass various health impacts. These include (i) impaired fetal growth i.e., low birth weight with postnatal catch-up growth, (ii) histopathological changes with notable oxidative stress and cell apoptosis, (iii) reproductive toxicity manifested through altered hormone levels, (iv) disturbed neurodevelopment and metabolomic responses, (v) cardiometabolic disorders, and (vi) abnormal immune system and inflammatory activities[98–109]. Cardiometabolic disorders involve hypertension, dysregulated lipid and amino acid pathways, altered glucose homeostasis, insulin resistance, thyroid dysfunction, excess adiposity, diabetes, and overweight/obesity. These effects contribute to the risks associated with growth and development and are closely linked to the disruption of the endocrine system, ultimately leading to increased mortality and morbidity. Moreover, in many cases, the effects of PFAS exposure exhibit potential sex-dependent variations, indicating sexual dimorphism in the biological response to exposure. Based on a search of the Scopus database, metabolic disruption has been the most extensively studied health outcome, followed by cell toxicity, and endocrine dysfunction (Fig. 5). Furthermore, the proportion of publications focusing on the health outcomes of PFOA and PFOS indicates a higher emphasis on PFOS exposure (47.8%) as compared to PFOA (38.6%).

Furthermore, the presence of mixture forms of contaminants, including parent compounds, metabolites, and other chemical pollutants, can result in combined effects. Kjeldsen and Bonefeld-Jørgensen[110] have reported additive and synergistic effects of PFAS mixture on androgen receptor function. In addition, antagonistic effects on neurotoxicity have been observed under co-exposure to PFOS and methylmercury[106]. The presence of bromine and/or chlorine in a PFAS mixture has been found to exert a stronger effect, a potentially additive effect on cell viability, leading to increased lipid peroxidation, altered gene expression associated with oxidative stress, and manipulated protein levels[111]. Furthermore, the microplastic and sorbed contaminants have significant combined effects towards homeostasis alteration[112]. The toxicity level in drinking water and human exposure via drinking water is a matter of concern, particularly when halogenated disinfection such as chlorination and bromination are commonly used in treatment processes. Synergistic effects of PFAS mixtures on gene expression, lipid metabolism, oxidative stress, epigenetic mechanisms, and the aryl hydrocarbon receptor pathway have also been observed in the presence of polychlorinated biphenyls[113]. Conversely, a study by Berg et al.[114] indicated equal toxicity of a mixture of PFAS and other persistent organic compounds, such as polychlorinated biphenyls and pesticides, on thyroid hormone homeostasis during pregnancy (no synergism), suggesting that the effects of individual compounds may be masked. While statistical methods for assessing multipollutant models have been developed and applied, there is a need for

tools to efficiently evaluate and classify PFAS toxicity, particularly in experimental toxicology studies focusing on the sensitivity of cells, tissues, organs, and systems towards PFAS, as well as exploration of the molecular mechanisms of toxicity. However, conducting epidemiological studies in this field poses formidable challenges due to the broad scope of contaminants, difficulty in interpreting the effects of contaminant mixtures, the lack of an unexposed population as a control group, various exposure factors (source, geographic location, seasonal variation, contamination level and dosage, exposure duration, and demographic factors), the complexity of contaminant mixtures and their interactions, as well as the complexity of the human body system.

DRINKING WATER REGULATION AND TREATMENT

The adoption of the regulation, guidance, and advisory values varies based on exposure considerations, including the drinking water ingestion rate on a body weight basis (L/kg/day), Relative Source Contribution (percentage of exposure to drinking water relative to total exposure from all sources), and toxicokinetic considerations[115]. In the absence of enforceable federal limits on PFAS, several states have taken the initiative to establish more stringent guidelines, standards, regulations, or legislations to address PFAS contamination in drinking water since 2019, although only a few PFAS compounds have been selected for regulation. The US EPA introduced stricter standards for PFAS in drinking water in 2022, with interim updated lifetime health advisory levels of 0.004 ng/L for PFOA and 0.02 ng/L for PFOS[116]. More recently, the US EPA proposed a National Primary Drinking Water Regulation, recommending enforceable maximum contaminant levels of 4 ng/L for PFOA and PFOS in drinking water in March 2023[117]. At the European Union level, the recast of the Drinking Water Directive, which serves as the primary legislation governing drinking water within the European Union, introduced a regulatory limit of 500 ng/L for total PFAS in January 2021. Most of the measured levels of PFOA and PFAS in drinking water (Fig. 4) were below the regulatory compliances for drinking water (Fig. 6), with comparatively higher concentrations observed in the United States, United Kingdom, Sweden, Ghana, and Brazil. Figure 6 shows the trend of guidelines, standards, regulations, or legislation aimed at addressing PFAS in drinking water. PFAS regulation, guidance, and advisory values are periodically updated by the Interstate Technology and Regulatory Council[7].

Simultaneously, several states and countries have implemented drinking water standards that directly impact groundwater quality. For example, in Alaska, Connecticut, Illinois, Vermont, New Hampshire, Michigan, Minnesota, and Denmark, immediate measures are being taken to control groundwater quality. As per the US EPA's recommendation, the preliminary remediation goal for contaminated groundwater that serves as a drinking water source (both current and potential) is the lifetime drinking water health advisory level of PFOA and PFOS, which is set at 70 ng/L. However, this goal may be adjusted on a site-specific basis as more information becomes available. The Wisconsin Department of Health Services is also actively working on establishing groundwater standards for PFAS. In contrast, governance of PFAS in surface water is relatively limited. The Oregon Department of Environmental Quality has set initiation levels of 24 µg/L for PFOA and 300 µg/L for PFOS in surface water. The Michigan Department of Environment, Great Lakes, and Energy recommend a maximum level (human non-cancer value for surface drinking water) of 420 ng/L for PFOA and 11 ng/L for PFOS in surface water used for drinking purposes, which is stricter compared to non-drinking water sources (PFOA: 12 µg/L; PFOS:12 ng/L). The Minnesota Department of Health regulates only PFOS in surface water based on health-based value (lake: 12 ng/L; river: 6 ng/L). The Alaska Department of Environmental Conservation and Colorado's Water Quality Control Commission have established an action level 70 ng/L for PFAS individually and in combination. Recently, the legislature in Wisconsin approved the Surface Water Quality Criteria rule, which includes a level of public health significance of 20 ng/L for PFOA and 8 ng/L for PFOS.

The majority of conventional treatment processes have shown to be ineffective in removing PFAS, whereas reverse osmosis, anion exchange, and granular activated carbon techniques have proven to be effective in removing PFAS, with reverse osmosis capable of removing both long- and short-chain PFAS, and anion exchange and granular activated carbon effective against longer-chain PFAS[118]. The removal of PFOA and PFOS by different treatment technologies in drinking water treatment plants is summarized in Table 1. Remarkably, granular activated carbon has a lower removal rate, or adsorption capacity, compared to powder activated carbon due to its larger particle size, which results in a lesser surface area, lesser surface functional groups, fewer active adsorption sites, longer internal diffusion distances, and the rigidity of the CF_2 bond[6,119]. Additionally, granular activated carbon requires frequent reactivation to maintain its removal efficiency[6]. The relatively high abundance of PFOA and PFOS in effluent water is attributed to the low removal efficiency of the treatment technologies employed in drinking water treatment plants, including pH adjustment, pre-oxidation, coagulation, flocculation, decantation, sand filtration, post-oxidation, granular activated carbon, and chlorination, with removal efficiencies reported at 33.3% and 10.1%, respectively[120]. Moreover, a negative removal rate was observed, where the concentration of PFOA in treated water is higher than that in the corresponding raw water[71,119] (Table 1). The increase in the concentration of PFAS, including PFOA, PFOS, and other short-chain PFAS, can be attributed to precursor transformation occurring during the treatment process, which is potentially enhanced by the presence of radicals such as nitrate-specific radicals and hydroxyl radicals[121]. The isomeric distribution in raw water sources can influence the overall efficiency of the treatment process, as observed with branched isomers of PFOS exhibiting higher reactivity and lower sorption compared to linear isomers[70]. Conversely, the superior removal rate of PFOS compared to PFOA with the same chain length can be attributed to the additional C–F bond in PFOS, which enhances its hydrophobic properties and sorption[36]. The strong C–F bond and electron-withdrawing functional groups (−COOH and $-SO_3H$) in PFOA and PFOS, respectively, contribute to their resistance to oxidation, including by molecular ozone and hydroxyl radicals[6]. Reverse osmosis has shown the ability to remove ≥ 99% of PFOA and PFOS, and the incorporation of advanced treatment technology has improved the efficiency of conventional treatment technology, increasing the removal of PFOA and PFOS from 52 ± 31% and 69 ± 12%, respectively, to 89 ± 22% and 86 ± 7%, respectively[120]. Moreover, this technology has successfully reduced the concentration of PFOA and PFOS in accordance with most drinking water regulatory standards, bringing the levels from < 4.2–30 to < 4.2–5.5 ng/L for PFOA, and from 6.9–71 to 3.0–21 ng/L for PFOS (Fig. 6).

Recently, Wang et al.[122] reported the excellent adsorption capacity of magnetic nanoparticles-attached fluorographene-based sorbent for PFOA and PFAS removal, surpassing activated carbon, with high removal efficiencies of 92–95% for PFOA and 94–97% for PFOS, effectively reducing their concentrations in the environment (~5 µg/L) to below 50 ng/L. Nasir et al.[123] proposed the use of agro-biomass biochar as a natural adsorbent for the removal of emerging organic contaminants, including PFAS. Moreover, the utilization of advanced materials such as metal-organic frameworks (MOFs) for the remediation of PFAS-contaminated water has gained attention. MOFs exhibit tunable properties, hierarchical structure, immense pore volume and surface area, design flexibility, and regenerability, making them a promising approach for safe and environmentally friendly PFAS removal[124,125]. Several studies have demonstrated the efficacy of

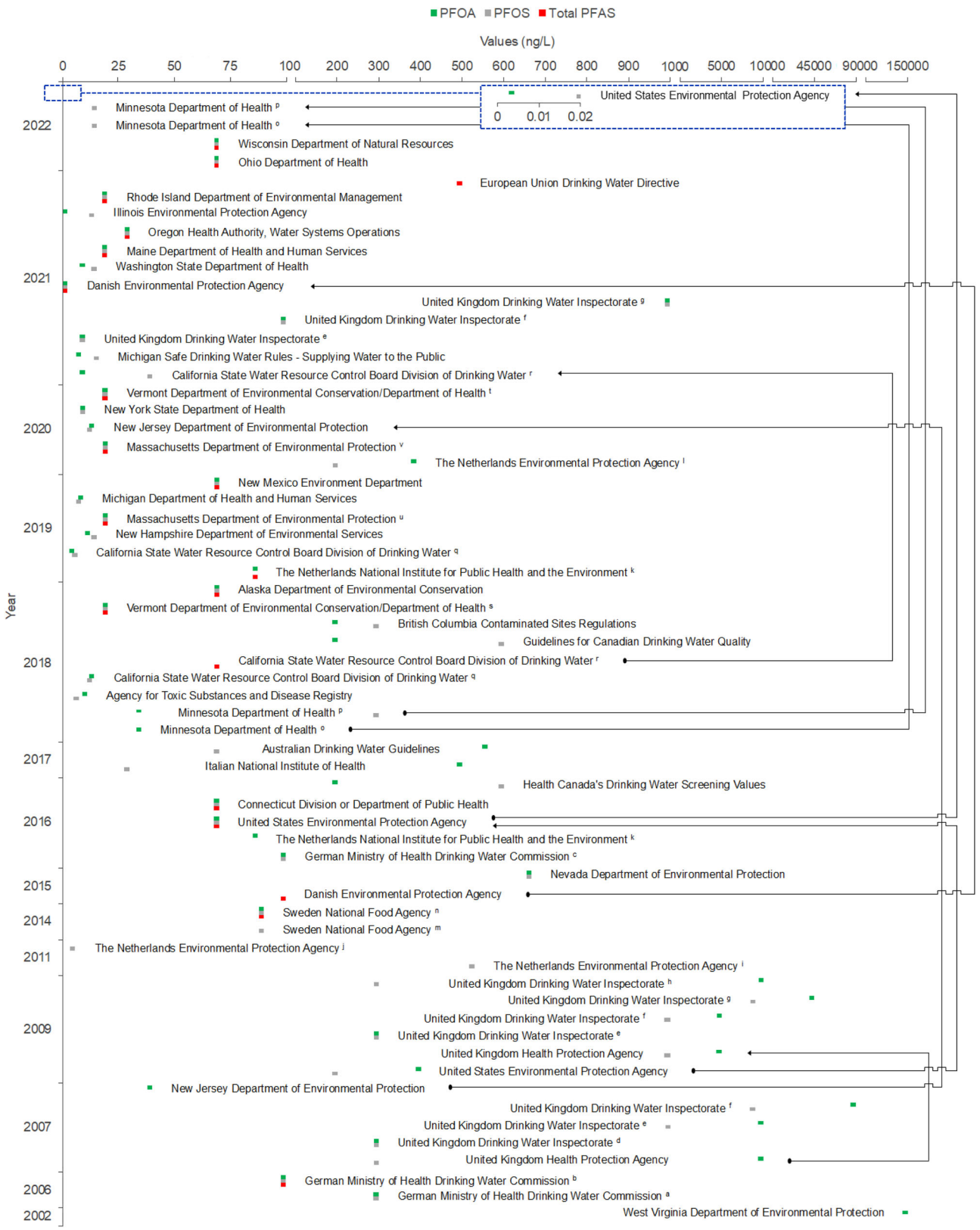

PFOA PFOS Total PFAS
Values (ng/L)
0 25 50 75 100 200 300 400 500 600 700 800 900 1000 5000 10000 45000 90000 150000
0 0.01 0.02
United States Environmental Protection Agency
Minnesota Department of Health P
Minnesota Department of Health O
Wisconsin Department of Natural Resources
Ohio Department of Health
European Union Drinking Water Directive
Rhode Island Department of Environmental Management
Illinois Environmental Protection Agency
Oregon Health Authority, Water Systems Operations
Maine Department of Health and Human Services
Washington State Department of Health
Danish Environmental Protection Agency
United Kingdom Drinking Water Inspectorate G
United Kingdom Drinking Water Inspectorate F
United Kingdom Drinking Water Inspectorate E
Michigan Safe Drinking Water Rules - Supplying Water to the Public
California State Water Resource Control Board Division of Drinking Water R
Vermont Department of Environmental Conservation/Department of Health T
New York State Department of Health
New Jersey Department of Environmental Protection
Massachusetts Department of Environmental Protection V
The Netherlands Environmental Protection Agency I
New Mexico Environment Department
Michigan Department of Health and Human Services
Massachusetts Department of Environmental Protection U
New Hampshire Department of Environmental Services
California State Water Resource Control Board Division of Drinking Water Q
The Netherlands National Institute for Public Health and the Environment K
Alaska Department of Environmental Conservation
Vermont Department of Environmental Conservation/Department of Health S
British Columbia Contaminated Sites Regulations
Guidelines for Canadian Drinking Water Quality
California State Water Resource Control Board Division of Drinking Water R
California State Water Resource Control Board Division of Drinking Water Q
Agency for Toxic Substances and Disease Registry
Minnesota Department of Health P
Minnesota Department of Health O
Australian Drinking Water Guidelines
Italian National Institute of Health
Health Canada's Drinking Water Screening Values
Connecticut Division or Department of Public Health
United States Environmental Protection Agency
The Netherlands National Institute for Public Health and the Environment K
German Ministry of Health Drinking Water Commission C
Nevada Department of Environmental Protection
Danish Environmental Protection Agency
Sweden National Food Agency N
Sweden National Food Agency M
The Netherlands Environmental Protection Agency J
The Netherlands Environmental Protection Agency I
United Kingdom Drinking Water Inspectorate H
United Kingdom Drinking Water Inspectorate G
United Kingdom Drinking Water Inspectorate F
United Kingdom Drinking Water Inspectorate E
United Kingdom Health Protection Agency
United States Environmental Protection Agency
New Jersey Department of Environmental Protection
United Kingdom Drinking Water Inspectorate F
United Kingdom Drinking Water Inspectorate E
United Kingdom Drinking Water Inspectorate D
United Kingdom Health Protection Agency
German Ministry of Health Drinking Water Commission B
German Ministry of Health Drinking Water Commission A
West Virginia Department of Environmental Protection
Year
2022
2021
2020
2019
2018
2017
2016
2015
2014
2011
2009
2007
2006
2002

Fig. 6 Trend of guidelines, standards, regulations, or legislations addressing PFAS contamination in drinking water. Various stakeholders are taking the initiative to develop more stringent guidelines independently. [a]Health-based precautionary value; [b]Health-based guide value; [c]Guideline (TW_{LW}); [d]Tier 1; [e]Tier 2; [f]Tier 3; [g]Tier 4; [h]Health-based value; [i]Health-based value; [j]Administrative value; [k]Drinking water limit; [l]Indicative Levels for Severe Pollution; [m]Health-based value; [n]Administrative value; [o]Health risk limit—Subchronic; [p]Health risk limit—Chronic; [q]Notification level; [r]Response level; [s]Drinking water health advisory; [t]Maximum contaminant level; [u]Drinking water value; [v]Maximum contaminant level.

Table 1. Reported removal of PFOA and PFOS by various treatment technologies in drinking water treatment plants.

Treatment technology	Compound	Mean concentration (ng/L)		Removal efficiency (%)	Reference
		Raw water	Treated water		
pH adjustment (CO_2), pre-ozonation, coagulation, flocculation, decantation, sand filtration, post-ozonation, GAC, and chlorination (NaClO)	PFOA	0.51	0.34	33.3	[154]
	PFOS	0.69	0.62	10.1	
Pre-chlorination, sedimentation, and post-chlorination	PFOA	6.7	7.4	–	[71]
	PFOS	1.8	1.6	8.2	
Sedimentation and GAC	PFOA	6.7	ND	100	[71]
	PFOS	1.9	0.5	73	
Coagulation, sand filtration, ozonation, and GAC	PFOA	0.66	0.71	–	[119]
	PFOS	1.90	1.80	5.5	
Coagulation, sand filtration, and GAC	PFOA	5.00	4.20	30	[119]
	PFOS	4.99	5.20	38	
Coagulation, sand filtration, and PAC	PFOA	5.00	0.28	95	[119]
	PFOS	4.99	0.44	95	
Pre-chlorination, sand filtration, ozonation, GAC, and post-chlorination	PFOA	21	13	52	[120]
	PFOS	116	33	69	
Pre-chlorination, sand filtration, ozonation, GAC, UF, RO, post-chlorination	PFOA	6.9	3	89	[120]
	PFOS	86	13	86	

GAC granular activated carbon, *PAC* powder activated carbon, *UF* ultrafiltration, *RO* reverse osmosis, – negative removal efficiency.

MOFs in removing PFAS from aqueous solution[126–128]. However, the implementation of advanced treatment methods in drinking water treatment plants is a formidable challenge, particularly in countries where there is a lack of specific regulations and frequent changes in proposed guideline values. It is essential to consider factors such as removal efficiency, cost-effectiveness, process sustainability, and potential treatment by-products when evaluating these advanced treatment options. Therefore, there is a need to assess the efficacy and feasibility of PFAS removal technologies at a larger scale in real drinking water treatment plants, beyond laboratory-scale studies.

RISK ASSESSMENT

The establishment of regulatory compliance as a prescriptive approach poses perennial challenges, as it requires careful consideration of several factors, including background contamination levels, concrete evidence of adverse health impacts, and the costs and benefits analyzed through regulatory impact analysis. While human databases are preferable for accurately determining dose–response relationships and serving as the primary basis for drinking water guidelines, animal data are still commonly used for this purpose. In addition, exposure assessment and risk characterization can be employed as alternatives, alongside existing risk monitoring and management measures, to provide precautionary advice for water source protection, water supply security, environmental and human health risks, treatment efficiency, and contamination forecasting. These measures are closely tied to the development of risk behaviors such as preparedness, reduction, prevention, and mitigation. However, emerging contaminants still require extensive exploration by the scientific community in terms of their nature, characteristics, and evidences. Insufficient database poses a challenge in the risk assessment of emerging contaminants.

Not only are guidelines, standards, and regulations formulated, but provisional health-based guidance values are also adopted for risk assessment. The US EPA recommends a reference dose (RfD) of 20 ng/kg/day for PFOA and PFOS[129,130]. In risk characterization, the estimated exposure dose (EED) of the chemical is often calculated and compared to the respective RfD, whereby appropriate action should be taken when the EED exceeds the RfD. The regulatory dose (RgD) is also determined based on this assessment. Recently, the US EPA has developed a draft RfD, cancer slope factor (CSF), and relative source contribution (RSC) for PFOA and PFOS using human data, which would lead to much lower drinking water values[131]. In addition, the Agency for Toxic Substances and Disease Registry (ATSDR) draft a minimum risk level (MRL) of 3 ng/kg/day for PFOA and 2 ng/kg/day for PFOS, and these values serve as screening tools when both RfD and MRL values are similar from a toxicological standpoint[132]. Both RfD and MRL estimate the average daily human exposure to a chemical that is likely to pose no appreciable risk of adverse non-cancer health effects over a specified exposure duration. Furthermore, the RfD is commonly incorporated in the calculation of the hazard quotient (HQ) or hazard ratio (HR) for risk assessment of drinking water (Supplementary Fig. 1).

The exposure of different age groups in China, including infants (≤ 1 year old), children (2–5 years old), teenagers (6–17 years old), and adults (≥ 18 years old), to dominant PFAS, such as PFOA (0.06–0.12 ng/kg/day) and PFOS (0.04–0.08 ng/kg/day), through drinking water was associated with the low hazard, indicated by HQ values < 1[133]. Furthermore, the HR values indicated that the levels of PFOA and PFOS detected in China's groundwater were not likely to pose a significant risk (HR < 1) to residents through exposure to drinking water alone[134]. The concepts of health index (HI) and risk index (RI) methods are similar to HR. In Taiwan, drinking water posed a low risk (HI < 1) of PFOA, PFOS, and total PFAS when using the RfD values provided by the US EPA Health Advisory (20 ng/kg/day) or Minnesota Department of Health (PFOA: 18 ng/kg/day; PFOS: 3.1 ng/kg/day)[135]. However, the risk of individual PFOA increased to a high-risk level (HI > 1) when employing the stricter RfD values set by the New Jersey Department of Environmental Protection (PFOA: 2 ng/kg/day; PFOS: 1.8 ng/kg/day). Despite the highest RI associated with PFAS in drinking water from Brazil compared to those from France and Spain, drinking water consumption in all three countries may not

pose an immediate health risk (RI < 1) to all age groups of consumers[77]. The risk quotient (RQ) method is another deterministic approach commonly used for environmental and human health risk assessment[72,136–138]. In Guangzhou city, the predominant occurrence of PFOA and PFOS in tap water from drinking water treatment plants was deemed safe for drinking (RQ < 1), as reported with RQ values ranging from 10^{-3} to 10^{-2} [119].

Acceptable daily intake (ADI) or tolerable daily intake (TDI), which share the same concept as RfD and MRL, are important parameters for risk calculation. Food Standards Australia New Zealand (FSANZ)[139] sets the ADI or TDI at 160 ng/kg/day for PFOA and 20 ng/kg/day for PFOS, which are lower than the values recommended by the European Food Safety Authority (EFSA), namely 1500 and 150 ng/kg/day, respectively, which were adopted on an interim basis by enHealth in 2008. In 2018, EFSA introduced a new limit called tolerable weekly intake (TWI), which is set at 6 ng/kg/week for PFOA and 13 ng/kg/week for PFOS, whereby the converted TDIs are lower than those of FSANZ, and in 2020, EFSA further recommended a TWI of 4.4 ng/kg/week for a total of four PFAS (PFOA, PFOS, PFHxS, and PFNA)[139–141].

However, a broader approach and conceptual and practical changes are needed to go beyond the traditional toxicology study dogma in order to assess dose–response, long-term effects, windows of developmental vulnerability, mixture effects, and interaction with other stressors[98]. This is essential for understanding toxic reactions and assessing associated risks. Furthermore, the lack of advanced molecular biological approaches that utilize more sensitive endpoints led to an underestimation of the toxicity and environmental impact of PFAS, as traditional endpoints such as growth, reproduction, and mortality are currently being used[20]. Additionally, the isomer profile of the exposure source and the different toxicity of PFOS isomers influence the accuracy of the risk assessment. Yu et al.[19] reported an overestimation of PFOS risk in thyroid hormone when the isomer profile and the toxicity of individual isomers are not taken into account.

Human health risk assessment considers various factors such as age, daily water intake, and body weight. To reduce uncertainty and provide a conservative worst-case scenario, it is important to differentiate body weight and daily water intake based on specific life stages in human health life-stage risks[142]. Leung et al.[143] highlighted the lack of detailed information on drinking water intake and body weight of the local population, as human growth varies across countries[144]. Drinking water intake varies across regions and countries due to seasonal and climate variations[142,145]. Additionally, socio-demographic differences influence drinking water consumption patterns, leading to potential variations in exposure to waterborne hazards[81]. Therefore, for a better understanding of local exposures to the contaminants, data collection and analysis on the risk assessment derivatives such as contamination level, human morphology, drinking water consumption patterns, and household practices regarding tap water as drinking water should be carried out[11].

In China, infants (≤ 1 year of age), children (2–5 years of age), adolescents (6–17 years of age), and adults (≥ 18 years of age) have body weights of 9.1, 16.7, 42.1, and 60.6 kg, respectively, and daily water intakes of 0.59, 0.86, 1.33, and 1.85 L/day, respectively, with a frequency of exposure at 1[146]. Similarly, the population in Korea is divided into different age groups for exposure assessment based on age, physiological status, and consumption patterns. These groups include toddlers (> 2 years; 12.2 kg; 0.41 L/day), children (3–12 years; 26.0 kg; 0.72 L/day), adolescents (13–18 years; 58.2 kg; 0.97 L/day), and adults (≥ 19 years; 62.8 kg; 1.50 L/day), and the data on exposure factors were recently been updated[147,148]. In Japan, adults, both males (64.0 kg) and females (52.7 kg), have relatively low drinking water intake, approximately at 0.67 L/day[149]. The Malaysia database reflects different body weights and daily water intake of children (aged < 20 years) (25.3 kg; 1.26 L/day) and adults (aged ≥ 20 years) (68.4 kg; 1.86 L/day), with a frequency of exposure (365 days/365 days = 1)[72]. In the Oceania region, specifically, Australia, recommended water intake for males (85 kg) and females (70 kg) is 2 L/day, reflecting life expectancy[150]. Furthermore, there are gender variations in human morphology and drinking water consumption pattern, with males generally having higher body weight and water ingestion. Other than that, the EFSA Panel on Dietetic Products, Nutrition, and Allergies (NDA) recommends age-specific water intake values in Europe, including 0.8–1 L/day for infants aged 6–12 months, 1.1–1.2 L/day for children aged 1–2 years, 1.3 L/day for children aged 2–3 years,1.6 L/day for children aged 4–8 years, and 2.1 L/day for male and 1.9 L/day for female children aged 9–13 years[151]. Adolescents aged ≥ 14 years are classified as adults and have a recommended water intake of 2.5 L/day for males and 2.0 L/day for females. In cases where actual measured data is unavailable, the EFSA Scientific Committee provides default body weight values of 5 kg for infants aged 0–12 months, 12 kg for children aged 1–3 years, and 70 kg for adults[152]. Campestrini and Jardim[153] conducted a human health risk assessment based on the average weight of 70 kg and daily water intake of 2 L for a standard European adult, as recommended by the EFSA Scientific Committee[152].

NABC ANALYSIS

PFAS have emerged as contaminants in the water cycle, posing potential risks to human health through drinking water. Exposure to PFAS is often associated with a wide range of toxic effects, particularly related to endocrine dysfunction. However, due to limited epidemiological evidence, experimental toxicology studies, and mechanistic evidence, many of the specific functions, underlying mechanisms, and contributing factors remain poorly understood. The global contamination crisis involving PFAS in the environment and human exposure through drinking water is a complex issue that is unlikely to be resolved in the near future. Therefore, it is crucial to conduct longitudinal exposure assessments and comprehensive health risk evaluations to gain a better understanding of the prevalence and persistence of PFAS exposure. Additionally, there is a need to reevaluate the use of animal data in developing PFAS drinking water guidelines, as reliance on such data may lead to inadequate human risk assessment. Furthermore, the unmonitored and unregulated nature of PFAS in many countries worldwide is a serious concern, as the risk extends beyond the developmental status of a country and affects both affluent and impoverished nations. Therefore, it is imperative to conduct extensive monitoring efforts and risk assessments across continents, establish analytical methods, and implement global monitoring campaigns to create a comprehensive database that can inform regulations and control PFAS contamination and exposure. While advanced technologies have shown promise in effectively removing PFAS, challenges remain in achieving complete removal, ensuring process sustainability, and addressing cost-effectiveness. Incorporating advanced treatment methods poses an ongoing challenge, especially in developing and least developed countries (or low- and middle-income countries) where conventional treatment systems are commonly used, and some regions lack any treatment infrastructure. Effective monitoring and management of PFAS contamination and risk require active communication and participation from multiple stakeholders, including researchers, academicians, water technologists, industries, authorities, owners, managers, policymakers, and the public. Collaboration between the public and private sectors and civil society is essential. By working together, it is possible to establish effective monitoring systems and implement appropriate management strategies. Table 2 provides a summary of the Needs, Approaches, Benefits, and Challenges (NABC) associated with regulating and managing PFAS in the

Table 2. NABC analysis of PFAS contamination and exposure in drinking water.

Needs	Approaches	Benefits	Challenges
1. Longitudinal exposure assessment and comprehensive health risk evaluation.	Reappraisal of approaches to employing animal data in PFAS drinking water guidelines.	Regulating the contamination and exposure of PFAS.	Limited epidemiological evidence, experimental toxicology studies, and mechanistic evidence.
2. Extensive monitoring work and risk assessment.	Establishment of robust analytical methods and global monitoring campaigns for comprehensive database profiling.	Gaining insights into the nature and extent of PFAS contamination.	Lack of monitoring and regulation of PFAS in numerous countries.
3. Effective treatment materials and incorporation of advanced treatment.	Utilizing advanced technologies for efficient PFAS removal.	Enhancing the efficiency of PFAS removal.	Overcoming challenges related to complete removal, process sustainability, and cost-effectiveness.
4. Communication and participation of multiple stakeholders.	Facilitating collaboration among researchers, academicians, water technologists, industries, authorities, owners, managers, policy makers, and the public community.	Advancing environmental sustainability, economic growth, and public health.	Incorporating effective monitoring and management frameworks in developing and least developed countries.

environment and human exposure through drinking water. In short, the monitoring and management of PFAS contamination and exposure is a complex issue that demands a multi-pronged approach. One of the key aspects is promoting environmental sustainability by reducing pollution, utilizing resources sustainably, and implementing best practices. Investing in sustainable practices and technologies not only reduces pollution but also stimulates economic growth (improving operational efficiency, capital budgeting, and investment appraisals) and protects public health (ensuring safe access to water). Therefore, global stakeholders must unite and collaborate to effectively regulate and manage PFAS contamination and exposure, ultimately safeguarding the well-being of communities worldwide.

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S.Y.W.: conceptualization, formal analysis, visualization, writing—original draft, writing—review & editing; A.Z.A.: conceptualization, funding acquisition, writing—review and editing.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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